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Four-year Follow-up of the SYNTAX Trial: Optimal Revascularization Strategy in Patients with Left Main Disease

Patrick W Serruys[1], José M González-Santos[2], Ignacio Santos Rodriguez[2], Michael J Mack[3], Ted E Feldman[4], A. Pieter Kappetein[1], Antonio Colombo[5], David R Holmes[6], Elisabeth Stahle[7], Marie-Claude Morice[8], Keith D Dawkins[9], Friedrich W Mohr[10]
[1]Erasmus University Medical Center Rotterdam, Rotterdam, Netherlands; [2]Hospital Clinico Salamanca, Salamanca, Spain; [3]Heart Hospital Baylor Plano, Plano, TX; [4]Evanston Hospital, Evanston, IL; [5]San Raffaele Scientific Institute, Milan, Italy; [6]Mayo Clinic, Rochester, MN; [7]University Hospital Uppsala, Uppsala, Sweden; [8]Institut Hospitalier Jacques Cartier, Massy, France; [9]Boston Scientific Corporation, Natick, MA; [10]Herzzentrum Universität Leipzig, Leipzig, Germany

Background: The optimal revascularization strategy for left main (LM) disease in the era of drug-eluting stents has become controversial. Consensus guidelines recommend coronary artery bypass graft surgery for the treatment of significant de novo LM stenosis; however, the recommendation for unprotected left main coronary artery (ULMCA) percutaneous coronary intervention has recently received a Class IIb indication. This analysis will focus on outcomes of LM patients (pts) in the SYNTAX trial at 4 years.
Methods: SYNTAX randomized pts with de novo 3 vessel (3VD) and/or LM disease to PCI with TAXUS Express stents or CABG if suitable for equivalent revascularization using either treatment. Analysis of this unprotected LM cohort was prespecified and sufficiently powered.
Results: Three-year MACCE and the composite of death/stroke/MI were similar in ULMCA- PCI and CABG-treated pts (Table). Stroke was significantly increased in the CABG group and repeat revascularization was increased in the PCI arm at 3 years (Table). MACCE was similar between groups in pts with lower SYNTAX Scores (0-32: 23.2% vs 20.5%, p=0.45) but significantly increased in PCI pts with high scores (≥33: 21.2% vs 37.3%, p=0.003).

Adverse Event Rates in the LM cohort at 3 years

		CABG	PCI		CABG	PCI
3-year Rates	MACCE	22.3	26.8	Stroke	4.0*	1.2
	Death/Stroke/MI	14.3	13.0	MI	4.1	6.9
	Death	8.4	7.3	Repeat Revascularization	11.7	20.0*

MACCE: Major adverse cardiac and cerebrovascular events including all-cause death, stroke, MI, repeat revascularization. Time-to-event rates at 3 years. *p<0.05 from log-rank or chi-square test.

Conclusion: At 3-years, no difference in MACCE was found between groups. There was an advantage of PCI in stroke; a benefit in the need for reintervention was still found in CABG. SYNTAX and other recent studies of LM disease suggest that in some pts, PCI using drug-eluting stents may be as effective but less invasive than CABG.

TCT-50

Complex Coronary Bifurcation Lesions Treated with the Novel Polymer-Free Dedicated Bifurcation Paclitaxel-Eluting Stent (Nile Pax): 9-Month Clinical and Angiographic Results of the Prospective, Multicenter BIPAX Clinical Trial

Ricardo A Costa[1, 2], Alexandre Abizaid[1, 2], Andrea S Abizaid[2], Bruno Garcia[3], Jacques Berland[5], Ivo Petrov[4], Phillipe Brenot[6], Patrick Serruys[7], Paolo Rubino[9], Thierry Royer[8], Maciej Lasiak[10], Jean Fajadet[11]
[1]Invasive Cardiology, Instituto Dante Pazzanese de Cardiologia, Sao Paulo, Brazil; [2]Cardiovascular Research Center, Sao Paulo, Brazil; [3]Hospital Universitari Vall D Hebron, Barcelona, Spain; [4]Tokuda Hospital, Sofia, Bahamas; [5]Clinique Saint Hilaire, Rouen, France; [6]Centre Cardiologique d Evecquemont, Evecquemont, France; [7]Thorax Center Erasmus University, Rotterdam, Netherlands; [8]Centre Cardiologique du Nord, Saint Denis, France; [9]Casa di Cura Montevergine, Mercogliano, Italy; [10]Karol Marcinkowski University of Medical Sciences, Poznan, Poland; [11]Clinique Pasteur, Toulose, France

Background: The Nile PAX® dedicated drug-eluting stent (Minvasys SAS, France) is a novel technology designed for percutaneous treatment of coronary bifurcation lesions with a provisional approach that incorporates: 1. a cobalt-chromium alloy designed to optimize scaffold of the bifurcation carina with maintenance of side branch (SB) access without need for rewiring (Nile CroCo® platform, Minvasys SAS, France); 2. a non-polymeric coating (PAX) technology; and 3. a potent antiproliferative agent (paclitaxel).
Methods: From Dec/08 to Mar/09, a total of 101 pts with single bifurcation lesion were prospectively enrolled in this non-randomized, multicenter (10 sites in Europe/South America) study. Lesion criteria were vessel size 2.5-3.5mm in the parent vessel (PV) and 2.0-3.0mm in the SB, and lesion length <14mm in the PV.
Results: LAD/Dg was the most prevalent location (75%), and 60% had significant involvement of both branches. In the procedure, PV was predilated in 97%; the study stent was successfully attempted and implanted in 99%. Overall, 25% of SB received an additional stent; and 94% of lesions had final kissing-balloon inflation. Angiographic success (residual stenosis <50%, final TIMI 3 flow, and absence of dissection) was achieved in 98%. There was only 1 major adverse cardiac event during hospitalization, which was adjudicated as a non-Q myocardial infarction during hospitalization, and no additional adverse events were reported up to 30 days. At 9 months, binary restenosis (primary endpoint) was 13.8% in the PV and 12.6% in the SB, and clinical outcomes included 8.4% clinically-driven target lesion revascularization (TLR) and no occurence of death or stent thrombosis.
Conclusion: The novel Nile PAX dedicated bifurcation polymer-free technology demonstrated excellent performance in the treatment of complex bifurcation lesions, including high procedural success and no events from discharge to 30 days FU. Up to 9-month FU, there were no cardiac death nor stent thrombosis, and clinically-driven TLR was 8.4%.

Pharmacology

Room 122

Tuesday, November 8, 2011, 10:15 am - 12:25 pm

(Abstract nos 51 - 60)

TCT-51

Concomitant Clopidogrel and Statin Use and Risk of Major Adverse Cardiovascular Events Following Coronary Stent Implantation

Morten Schmidt[1, 2], Martin B Johansen[1], Michael Maeng[2], Anne Kaltoft[2], Lisette O Jensen[4], Hans-Henrik Tilsted[5], Hans E Bøtker[2], John A Baron[3], Henrik T Sørensen[1]
[1]Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark; [2]Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark; [3]Department of Medicine University of North Carolina School of Medicine, Chapel Hill, NC; [4]Department of Cardiology, Odense University Hospital, Odense, Denmark, Odense, Denmark; [5]Department of Cardiology, Aarhus University Hospital, Aalborg, Aalborg, Denmark

Background: The clopidogrel-statin interaction has not been examined using time-varying drug exposure ascertainment. We examined whether statin use modified the association between clopidogrel use and major adverse cardiovascular events (MACE) after coronary stent implantation.
Methods: We conducted this population-based cohort study in Western Denmark (population: 3 million) using medical databases. We identified all 13,001 patients with coronary stent implantation between 2002 and 2005 and their comorbidities. During 12-month follow-up, we tracked use of clopidogrel and statins and the rate of MACE. We used Cox regression to compute hazard ratios controlling for potential confounders.
Results: The rate of MACE per 1000 person years was 104 for concomitant clopidogrel and statin use, 129 for clopidogrel without statin use, 107 for statin without clopidogrel use, and 449 for no use of either drug. The adjusted hazard ratio comparing clopidogrel use with non-use was 0.68 (95% confidence interval: 0.58-0.80) among statin users and 0.34 (95% confidence interval: 0.29-0.40) among statin non-users, yielding an interaction effect (i.e., relative rate increase) of 1.99 (95% confidence interval: 1.61-2.47). The adjusted hazard ratio for MACE comparing statin use with non-use was 0.97 (95% confidence interval: 0.83-1.13) among clopidogrel users and 0.49 (95% confidence interval: 0.42-0.57) among clopidogrel non-users.
Conclusion: Clopidogrel and statin use was each associated with a substantially reduced rate of MACE within 12 months after coronary stent implantation. Although we observed an interaction between use of clopidogrel and statins, statin use vs. nonuse was not associated with an increased rate of MACE in patients using clopidogrel after coronary stent implantation.

TCT-52

Short-acting, Reversible Antiplatelet Therapy For Urgent Surgery Early After Coronary DES Implantation

Nuccia Morici[2], Stefano Savonitto[1], Stefano De Servi[2], Silvio Klugmann[1]
[1]Cardiology, Niguarda Hospital, Milano, Italy; [2]Ospedale Civile Legnano, Legnano, Italy

Background: Between 4 and 8% of pts need to undergo surgery in the first year after DES deployment. Dual antiplatelet therapy (DAPT) is associated with a 25% incidence of severe perioperative bleeding and is not protective against MACE, particularly in the early months after implantation. We hypothesized that i.v. short acting perioperative antiplatelet therapy using tirofiban during clopidogrel withdrawal would reduce the risk of D+MI+ST with no excess in bleeding.We used a Simon two-stage design to test the hypothesis that this approach would reduce the incidence of D+MI+ST from 30% to 5% (N=21)
Methods: Inclusion criteria:pts at high-risk for surgical bleeding within 12 months of DES implantation.Exclusion criteria: allergy to tirofiban (tir),stroke< 30 days,intracranial disease,trombocytopenia. At day -5 to surgery (surg) stop clopidogrel. At day -3 start tir (0,4 mg/kg/min over 30',followed by 0,1mg/kg/min). At -4h to surg stop tir. At +4h from surg resume tir. Resume clopidogrel as soon as oral administration is possible. Stop tir after 1 day.ASA continued throughout.Primary EP: the composite of death,MI,ST,haemostatic reoperation. Secondary EP: TIMI major bleeding.
Results: 56 pts enrolled in the bridge- therapy study for urgent surgery (surg) 4 days-12 months from DES implantation (median 3 months).In 19 pts cardiovascular surg,

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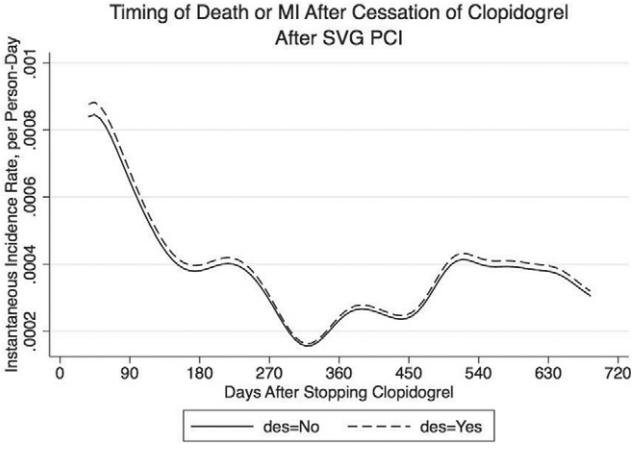
in 37 non cardiovascular (urinary tract 7 pts, gastrointestinal 18 pts,mixed surg 12). Primart EP :0 (97,5% CI 6,4%). Bleeding events : 2 major, according TIMI criteria (gastrointesinal surg), 2 minor, trasfusion in 11 pts. Severe thrombocitopenia (platelet count < 20.000): 1 pt.
Conclusion: Based on the results of our prospective study we propose that a "bridge strategy" using short-acting i.v. antiplatelet agents confers protection against perioperative CV events that goes beyond the prevention of stent thrombosis, without increasing the risk of bleeding, in pts in DAPT, planned for urgent surgery < = 12 months after DES implantation.

TCT-53

Death and Acute Myocardial Infarction Associated with Stopping Clopidogrel After Saphenous Vein Graft Percutaneous Coronary Intervention

Amit Sachdeva[1], Sumati Bavisetty[1], Gerald Beckham[1], Prakash Mansukhani[1], Vicken Aharonian[1], Gregg W Stone[2], Naing Moore[1], Ric Hyett[1], Richard Contreras[1], Somjot S Brar[1]
[1]Regional Cardiac Cath Lab, Kaiser Permanente, Los Angeles, CA; [2]Columbia University, New York, NY

Background: It remains unknown whether high-risk cohorts undergoing percutaneous coronary intervention (PCI) are at an increased risk of adverse events after clopidogrel cessation. We assessed the rates of adverse events after stopping clopidogrel treatment in patients who had undergone saphenous vein graft (SVG) PCI.
Methods: We identified patients undergoing SVG PCI between 2000-2009 in an integrated pre-paid health care plan. Clopidogrel utilization was ascertained from pharmacy records. The date of the prescription and quantity of tablets dispensed were recorded for every clopidogrel prescription filled by the patient post-PCI. A multivariate Cox regression model was constructed to obtain risk-adjusted instantaneous incidence rates using kernel hazard functions. The following covariates were included in the model: age, gender, comorbidities, clopidogrel duration and non-compliance, and use of concomitant medications (beta blockers, statins, and others).
Results: Among 603 patients who underwent SVG PCI during the study period, 403 were event free at the time of clopidogrel cessation and comprised the study cohort. Risk-adjusted instantaneous incidence rates for death or myocardial infarction after stopping clopidogrel treatment are shown in the figure. The risk of an adverse event appears to be greatest early after cessation of clopidogrel therapy, regardless of stent type.



Conclusion: A clustering of events was observed in the near-term after clopidogrel cessation in patients treated with either drug-eluting or bare metal stents. Additional studies are needed to confirm these findings and determine the responsible mechanisms.

TCT-54

The impact of High Residual Platelet Reactivity After Clopidogrel Loading on Long-Term Clinical Outcome of Patients with Acute Coronary Syndromes Receiving an Invasive Treatment. The RECLOSE 2-ACS trial

Renato Valenti, Guido Parodi, Angela Migliorini, Rossella Marcucci, Piergiovanni Buonamici, Giampaolo Cerisano, Guia Moschi, Gianfranco Gensini, Rosanna Abbate, David Antoniucci
Division of Cardiology, Careggi Hospital, Florence, Italy

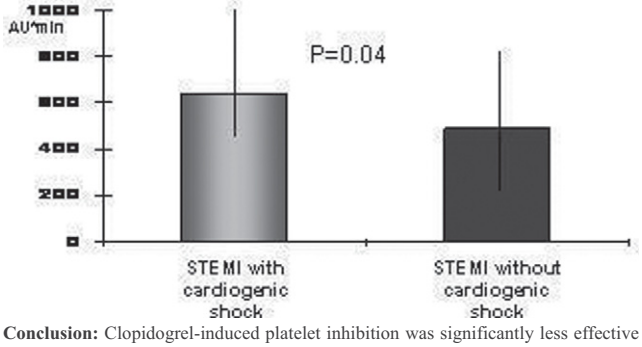
Background: Context High residual platelet reactivity (HRPR) on clopidogrel has been associated with high risk of ischemic events after percutaneous coronary intervention (PCI). To test the hypothesis that HRPR after clopidogrel loading would be an independent prognostic marker of risk of long-term thrombotic events in patients with acute coronary syndrome (ACS) receiving an invasive treatment and antithrombotic treatment adjusted according to the results of platelet function tests.
Methods: Prospective, observational, referral center cohort study of 1789 consecutive ACS patients undergoing PCI from April 2005 to April 2009, and for whom platelet reactivity was prospectively assessed by light transmittance aggregometry. Patients with HRPR by ADP test (≥ 70%) received an increased dose of clopidogrel (from 150 mg/daily to 300 mg/daily), or shifted to ticlopidine (500mg/daily to 1000 mg/daily), under ADP test guidance (clinicaltrials.gov Identifier: NCT01231035). The primary end point was the composite of cardiac death, myocardial infarction, any urgent coronary revascularization, and stroke at 2-year follow-up. Secondary end points were stent thrombosis, and each component of the primary end point.
Results: The primary end point rate was 14.6% in the HRPR group and 8.7% in the low residual platelet reactivity group (p = 0.003). Stent thrombosis rate was higher in the HRPR group as compared to the low residual platelet reactivity group (6.1% vs 2.9%, p = 0.001). By multivariable analysis, HRPR was an independent predictor of the primary end point (HR1.49, 95% CI 1.08-2.05, p = 0.015) and of cardiac mortality (HR 1.81, 95% CI 1.18-2.76, p = 0.006).
Conclusion: HRPR is a strong predictor of short- and long-term ischemic events, including stent thrombosis. Antiplatelet therapy using increased maintenance dose of clopidogrel or ticlopidine, has no impact on clinical outcome.

TCT-55

Is clopidogrel enough for STEMI patients with cardiogenic shock?

Klaus Tiroch[1, 2], Dirk Sibbing[2], Isabelle Bernlochner[2], Melchior Seyfarth[1], Adnan Kastrati[1]
[1]Herzzentrum, Wuppertal, Germany; [2]Herzzentrum, Munich, Germany

Background: ST-elevation myocardial-infarction (STEMI) patients show an attenuated platelet inhibition to clopidogrel 600 mg-loading dose. It could be hypothesized that STEMI patients with cardiogenic shock may even respond worse to standard clopidogrel loading. Thus, the aim of this study was to compare platelet inhibition in STEMI patients with and without cardiogenic shock after clopidogrel loading.
Methods: In this study, 237 consecutive STEMI patients (207 without cardiogenic shock and 30 with cardiogenic shock) were evaluated regarding their platelet inhibition using the Multiplate analyzer. Cardiogenic shock was defined as hemodynamic instability with need for catecholamines or intubated patients with clopidogrel 600mg-loading over nasogastric tube. We further assessed the number of primary clopidogrel low-responders (defined as >468 AU*min) and their response to an additional clopidogrel 600 mg-loading, and if necessary, to a further prasugrel 60 mg-loading.
Results: Platelet inhibition after clopidogrel 600 mg-loading was less effective for STEMI patients with cardiogenic shock (median 643 AU*min, interquartile range 448-1009) compared to those without cardiogenic shock (median 492 AU*min, interquartile range 222-822) (P=0.04). Platelet inhibition after prasugrel 60 mg-loading was highly effective in primary clopidogrel low responders.



Conclusion: Clopidogrel-induced platelet inhibition was significantly less effective for STEMI patients with cardiogenic shock compared to those without cardiogenic shock. Prasugrel was effective in primary clopidogrel low responders and may represent a better choice for STEMI patients with cardiogenic shock leading to highly activated platelets and impaired resorption and metabolization.

TCT-56

Impact of Major Bleeding on Long term Mortality in patients with and without Anemia Undergoing Percutaneous Coronary Intervention with Bivalirudin

Shyam Poludasu[1], Usman Baber[1], Avery E Clark[2], Rebecca Pinnelas[3], George Dangas[1], Roxana Mehran[1], Annapoorna S Kini[1], Samin K Sharma[1]
[1]Interventional Cardiology, Mount Sinai Medical Center, New York, NY; [2]Middlebury College, Vermont, VT; [3]New Jersey medical school, New Jersey, NJ

Background: Bleeding complications after percutaneous coronary intervention (PCI) have been associated with increased mortality. These data have been derived in the context of using Bivalirudin (BIV) versus heparin + GPIIb/IIIa inhibitors after PCI and especially STEMI. We studied the predictors of mortality after PCI in a population treated exclusively with BIV and we investigated the role of anemia on clinical outcomes.
Methods: We evaluated 11,991 patients who underwent PCI from July 2001 to May 2010 with bivalirudin as the primary antithrombotic agent. Bleeding complications were prospectively collected and defined by the criteria used in The Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction

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